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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/926,442	01/22/2002	Roger Nitsch	P67214US0	4254

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EXAMINER	
HAYES, ROBERT CLINTON	

ART UNIT	PAPER NUMBER
1647	9

DATE MAILED: 09/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/926,442	Applicant(s) Nitsch et al
	Examiner Robert C. Hayes, Ph.D.	Art Unit 1647

-- Th MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 4, 2003*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above, claim(s) *22-26* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-21* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1-26* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election of Group I (claims 1-21) in Paper No. 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 22-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 8.

Claim Rejections - 35 U.S.C. § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 3 is rejected under 35 U.S.C. 101 because the claimed recitation of "[u]se of..." , without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 U.S.C. § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for prognosing/predicting possible "increased risk of developing Alzheimer's disease" in patients suspected of having the disease clinically (e.g., having specific MMS scores) when using a specifically defined antibody preparation to NGF and NT-3, does not reasonably provide enablement for diagnosing Alzheimer's disease using a single "neurotrophin", or for any method using unknown and uncharacterized antibody preparations that are not further compared to appropriate reference/specifically defined age matched control values, etc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

First, different antibody preparations possess different detection limitations and/or detect different control levels inconsistent with a detection of "at least 4 pg NGF/ml" as being indicative of Alzheimer's disease, in general. For example, Massaro et al (1994; IDS Ref #: M) showed no detection of NGF in CSF from Alzheimer's patients (pgs.106-107), while Murase et al (1993; IDS Ref #: L) alternatively observed 7.27 ± 3.96 pg NGF/ml in normal control CSF and Nishio et al., 1998; IDS Ref #: I; pgs. 95-96; Table 1) observed control/reference levels

at 18.7± 3.3 pg NGF/ml. Second, many other neurological disorders give rise to NGF values of "at least 4 pg NGF/ml" (e.g., see Nishio et al, Table 1) or NT-3 levels ≥ 15 pg/ml (e.g., Gilmore et al., 1997; pg. 111, Table 1), in which the claims further recite no "suitable cut-off criteria" for prognosing Alzheimer's disease, as illustrated on page 11 of the specification (i.e., as it relates to claims 4, 13, 16 & 19). Moreover, even page 10 of the specification describes DE [major depression in the elderly] controls as having NGF levels of more than "4 pg NGF/ml" (i.e., as it relates to claims 4-5 & 15-16). In other words, no reasonable correlation exists within the art for directly correlating increased NGF levels, etc. as indicative of Alzheimer's disease, versus some other neurological disease state (i.e., as it relates to claims 1, 2, 8, 10, 11, 14 & 17), or for correlating some undefined "further neurotrophin" as indicative of Alzheimer's disease (i.e., as it relates to claims 11 & 17). Thus, because different antibody preparations reasonably and generically have different detection limitations for any given "neurotrophin", different "reference values" reasonably exist for different "known health status", as currently recited in the claims, one of ordinary skill in the art would not reasonably know how to make and use Applicants' invention, as currently claimed, without requiring undue experimentation to determine what parameters actually work in the claimed method.

Lastly, because everyone is potentially at risk for developing Alzheimer's disease (e.g., see page 1 of the specification), and because Scinto et al (1993) teach that "[c]urrently Alzheimer's disease... can only be definitively diagnosed by histological examination of brain tissue obtained at autopsy or biopsy" (see Abstract of Scinto et al, 1994), claim limitations

related to "diagnosis" based solely on one or two neurotrophic factors which are also altered in other neurological disease states (e.g., see Nishio et al), are further not reasonably enabled. For example, Applicants' own data on page 10 of the specification would indicate no "diagnose" in those patients with 0.00 and 3.29 pg NGF/ml, who otherwise are clinically indicated as having Alzheimer's disease. Additionally, even Applicants combined NGF and NT-3 levels putatively confirmed only 90.1% of the patients as having Alzheimer's disease (see pg. 11 of the specification). In other words, claim limitations related to "diagnosis", absent histological analysis, are not reasonably enabled; consistent with the state of the art at the time of filing Applicants' invention as illustrated by Scinto et al .

4. Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is ambiguous what exactly the recitation a "reference value representing a known disease or health status" means in that no "known disease or health status" is stated in the claims for determining what constitutes such a "reference value", and in which what exactly the "reference value" constitutes is also ambiguous and undefined.

Second, since claims 4, 13 & 19 fail to define a "reference sequence" it is ambiguous whether a "reference value" of $\geq$ 4 pg/ml, or $\geq$ 15 pg/ml, respectively, also "indicates a

diagnosis..."; especially as it relates to putative control subjects who may eventually be "at increased risk of developing Alzheimer's disease (e.g., see pg. 1 of the specification).

Third, in that Alzheimer's disease is a disease state unique to humans, it is indefinite what claim 6 is intended to claim that is separate and distinct from base claim 1.

5. Claims 5 & 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as", and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

In the present instance, claims 5 & 16 recite the broad recitation of "in the range from 4 pg/ml to 25 pg/ml", and the claims also recite "*in particular* in the range from 4 pg/ml to 14 pg/ml [emphasis added]", which is the narrower statement of the range/limitation.

6. Claims 9-10 & 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

There is no proper antecedent basis for the recitation of "said sample gatherings" or "said treatment" from base claim 1 in claims 9 & 10.

Second, it is indefinite for what metes and bounds entail a "treatment" when no specific disease state to be "treated" is recited, and what parameters actually constitutes a "treatment" when no such treatable parameters are described within the specification, nor recited in claims 9-10 & 21.

7. Claims 14-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular, claims 14 & 17 are indefinite because it is ambiguous when exactly a reagent "selectively detects" versus not selectively detects. In other words, the recitation of "selectively detects" in claims 14 & 17 is a relative term which renders the claim indefinite. The

term "selectively detects" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

8. Claims 3 & 20-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3 & 20-21 provide for the use of "the method according to claim 1" or "for use in monitoring... ", but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. In addition, no process steps for how or when "evaluating treatment for Alzheimer's disease"/ "monitoring a progression of Alzheimer's disease"/ "monitoring the success or failure of a therapeutic treatment" are accomplished is recited; thereby, also being incomplete.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
September 15, 2003